(FILE 'HOME' ENTERED AT 13:33:32 ON 16 OCT 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, LIFESCI, SCISEARCH, TOXLINE, CABA, BIOTECHNO, CANCERLIT, ESBIOBASE' ENTERED AT 13:33:43 ON 16 OCT 2000

L1 4033 S IMPDH OR (INOSINE (W) MONOPHOSPHATE (W) DEHYDROGENASE?) OR (I
L2 24 S PYOGENES AND L1
L3 31 S L1 AND (STREPTOCOC? OR PYOGENES)
L4 7 DUP REM L3 (24 DUPLICATES REMOVED)
L5 66589 S (THREE (W) DIMENSIONAL (W) STRUCTUR?) OR (3D (W) STRUCTUR?) O
L6 0 S L1 AND L2 AND L5
L7 13789 S L5 AND ((CRYSTAL OR X-RAY OR (X(W)RAY)) (3W) STRUCTUR?)
L8 18 S L1 AND L3 AND ((CRYSTAL OR X-RAY OR (X(W)RAY)) (3W) STRUCTU
L9 3 DUP REM L8 (15 DUPLICATES REMOVED)
L10 0 S L4 AND L7
L11 3 S L4 AND ((CRYSTAL OR X-RAY OR (X(W)RAY)) (3W) STRUCTUR?)
L12 3 DUP REM L11 (0 DUPLICATES REMOVED)

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS
AN 1999:464100 CAPLUS
DN 131:83979
TI Method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** )
IN Collart, Frank R.; Huberman, Eliezer
PA The University of Chicago, USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9933996 | A1 | 19990708 | WO 1998-IB2109 | 19981223 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9915022 | A1 | 19990719 | AU 1999-15022 | 19981223 |
| PRAI US 1997-997758 | | 19971224 | | |
| WO 1998-IB2109 | | 19981223 | | |

AB This invention relates to methods to identify specific inhibitors of the purine nucleotide synthesis enzyme, ***IMPDH*** . ***IMPDH*** is an essential enzyme found in all free-living organisms from humans to bacteria and is an important therapeutic target. The invention allows the identification of specific inhibitors of any ***IMPDH*** enzyme which can be expressed in a functional form in a recombinant host cell. To illustrate the utility of the invention, the coding sequence of human and ***Streptococcus*** , ***pyogenes*** ***IMPDH*** were cloned into the pJF118EH expression vector. A variety of eukaryotic or prokaryotic host systems commonly used for the expression. . . prodn. Utilization of exogenous guanosine as a control component of the methods allows for the identification of inhibitors specific for ***IMPDH*** rather than other causes of decreased cell proliferation.

L4 ANSWER 2 OF 7 MEDLINE DUPLICATE 1
TI Characteristics and crystal structure of bacterial inosine-5'-monophosphate dehydrogenase.
AU Zhang R; Evans G; Rotella F J; Westbrook E M; Beno D; Huberman E; Joachimiak A; Collart F R
SO BIOCHEMISTRY, (1999 Apr 13) 38 (15) 4691-700.
Journal code: A0G. ISSN: 0006-2960.
AB ***IMP*** ***dehydrogenase*** ( ***IMPDH*** ) is an essential enzyme that catalyzes the first step unique to GTP synthesis. To provide a basis for the evaluation of ***IMPDH*** inhibitors as antimicrobial agents, we have expressed and characterized ***IMPDH*** from the pathogenic bacterium ***Streptococcus*** ***pyogenes*** . Our results show that the biochemical and kinetic characteristics of S. ***pyogenes*** ***IMPDH*** are similar to other bacterial ***IMPDH*** enzymes. However, the lack of sensitivity to mycophenolic acid and the Km for NAD (1180 microM) exemplify some of the differences between the bacterial and mammalian ***IMPDH*** enzymes, making it an attractive target for antimicrobial agents. To evaluate the basis for these differences, we determined the crystal. . . obtained with synchrotron radiation from the undulator beamline (19ID) of the Structural Biology Center at Argonne's Advanced Photon Source. S. ***pyogenes*** ***IMPDH*** is a tetramer with its four subunits related by a crystallographic 4-fold axis. The protein is composed of two domains:. . . flap as an essential catalytic element and indicate there are significant differences in the catalytic environment of bacterial and mammalian ***IMPDH*** enzymes. Comparison of the structure of bacterial ***IMPDH*** with the known partial structures from eukaryotic organisms will provide an explanation of their distinct properties and contribute to the design of specific bacterial ***IMPDH*** inhibitors

L4 ANSWER 3 OF 7 MEDLINE DUPLICATE 2
TI ***IMP*** ***dehydrogenase*** : mechanism of action and inhibition.
AU Hedstrom L
SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 545-60. Ref: 89
Journal code: C02. ISSN: 0929-8673.
TI ***IMP*** ***dehydrogenase*** : mechanism of action and inhibition.
AB ***Inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ) catalyzes the conversion of IMP to XMP with the concomitant reduction of NAD to NADH. This reaction is the rate-limiting step in guanine nucleotide biosynthesis. ***IMPDH*** is a proven target for immunosuppressive, anticancer and antiviral chemotherapy, and may also be a target for antimicrobial agents. ***IMPDH*** is activated by monovalent cations, and one monovalent cation binding site appears to have been identified. The mechanism of ***IMPDH*** involves formation and hydrolysis of a covalent enzyme intermediate (E-XMP*) in a reaction reminiscent of glyceraldehyde-3-phosphate dehydrogenase. Substrates bind to ***IMPDH*** in a random order, hydride transfer is fast and NADH release precedes hydrolysis of E-XMP*. The hydrolysis of E-XMP* is. . .

L4 ANSWER 4 OF 7 MEDLINE DUPLICATE 3
TI Differential signatures of bacterial and mammalian ***IMP*** ***dehydrogenase*** enzymes.
AU Zhang R; Evans G; Rotella F; Westbrook E; Huberman E; Joachimiak A; Collart F R
SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 537-43.
Journal code: C02. ISSN: 0929-8673.
TI Differential signatures of bacterial and mammalian ***IMP*** ***dehydrogenase*** enzymes.

AB ***IMP*** ***dehydrogenase*** ( ***IMPDH*** ) is an essential enzyme of de novo guanine nucleotide synthesis. ***IMPDH*** inhibitors have clinical utility as antiviral, anticancer or immunosuppressive agents. The essential nature of this enzyme suggests its therapeutic applications may be extended to the development of antimicrobial agents. Bacterial ***IMPDH*** enzymes show biochemical and kinetic characteristics that are different than the mammalian ***IMPDH*** enzymes, suggesting ***IMPDH*** may be an attractive target for the development of antimicrobial agents. We suggest that the biochemical and kinetic differences between. . . is a prerequisite for the rational identification of agents that specifically target the bacterial enzyme. We used sequence alignments of ***IMPDH*** proteins to identify sequence signatures associated with bacterial or eukaryotic ***IMPDH*** enzymes. These selections were further refined to discern those likely to have a role in catalysis using information derived from the bacterial and mammalian ***IMPDH*** crystal structures and site-specific mutagenesis. Candidate bacterial sequence signatures identified by this process include regions involved in subunit interactions, the. . . a secondary pattern of amino acid conservation associated with the major phylogenetic groups. Elucidation of the basis for this mammalian/bacterial ***IMPDH*** signature will provide insight into the catalytic mechanism of this enzyme and the foundation for the development of highly specific.

L4 ANSWER 5 OF 7 MEDLINE DUPLICATE 4
TI ***IMP*** ***dehydrogenase*** : structural aspects of inhibitor binding.
AU Goldstein B M; Colby T D
SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 519-36. Ref: 118
Journal code: C02. ISSN: 0929-8673.
TI ***IMP*** ***dehydrogenase*** : structural aspects of inhibitor binding.
AB ***Inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** , E.C. 1.1.1.205) is recognized as an important target for both antileukemic and immunosuppressive therapy. ***IMPDH*** catalyzes the NAD-dependent oxidation of inosine 5 monophosphate (IMP) to xanthosine 5 monophosphate. Several classes of ***IMPDH*** inhibitors are now in use or under development. These include agents that bind at either the substrate site (e.g. ribavirin. . . acid and thiazole-4-carboxamide adenine dinucleotide). All suffer from some degree of toxicity and/or susceptibility to metabolic inactivation. The finding that ***IMPDH*** exists as two isoforms, one of which (type II) is induced in tumor cells, has led to the search for potentially more effective isoform-specific agents. Recently, a number of crystal structures of ***IMPDH*** have become available. These include structures of the human type II, hamster, Tritrichomonas foetus, ***Streptococcus*** ***pyogenes*** and Borrelia burgdorferi enzymes. Each structure crystallizes as a tetramer of a/b barrels, with the active site located partly at. . .

L4 ANSWER 6 OF 7 MEDLINE DUPLICATE 5
TI Cloning, sequence analysis and expression of the group A ***streptococcal*** guaB gene encoding ***inosine*** ***monophosphate*** ***dehydrogenase*** .
AU Ashbaugh C D; Wessels M R
SO GENE, (1995 Nov 7) 165 (1) 57-60.
Journal code: FOP. ISSN: 0378-1119.
TI Cloning, sequence analysis and expression of the group A ***streptococcal*** guaB gene encoding ***inosine*** ***monophosphate*** ***dehydrogenase*** .
AB ***Inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ) is an essential enzyme in the biosynthesis of purines. We cloned a group A ***streptococcal*** (GAS) DNA fragment containing an open reading frame similar to other bacterial guaB genes encoding ***IMPDH*** . The GAS guaB consists of 1479 nucleotides encoding a protein of 493 amino acids. Expression of the GAS guaB in an Escherichia coli guaB mutant restored ***IMPDH*** activity, confirming the function of the gene product and demonstrating that the GAS enzyme is active in a heterologous bacterial. . .

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2000 ACS
TI A simple method for the rapid determination of the stereospecificity of NAD-dependent dehydrogenases applied to mammalian ***IMP*** ***dehydrogenase*** and bacterial NADH peroxidase
AU Cooney, David; Hamel, Ernest; Cohen, Marvin; Kang, Gil J.; Dalal, Maha; Marquez, Victor
SO Biochim. Biophys. Acta (1987), 916(1), 89-93
CODEN: BBACAQ; ISSN: 0006-3002
TI A simple method for the rapid determination of the stereospecificity of NAD-dependent dehydrogenases applied to mammalian ***IMP*** ***dehydrogenase*** and bacterial NADH peroxidase.
AB The stereospecificity of ***IMP*** ***dehydrogenase*** (EC 1.1.1.205) from 2 different sources was detd. The enzyme prepns. were obtained from murine lymphoblasts and from Escherichia coli.. . . the enzyme from 2 very different species. In addn., the studies described here demonstrated that alc. dehydrogenase and NADH peroxidase ( ***Streptococcus*** faecalis), used as auxiliary enzymes, in combination with a microdistn. procedure, may rapidly det. the stereospecificity of any NAD-dependent dehydrogenase. . .

L9 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AN 1999218077 MEDLINE
DN 99218077
TI Characteristics and ***crystal*** ***structure*** of bacterial inosine-5'-monophosphate dehydrogenase.
AU Zhang R; Evans G; Rotella F J; Westbrook E M; Beno D; Huberman E; Joachimiak A; Collart F R
CS Center for Mechanistic Biology and Biotechnology, Argonne National Laboratory, 9700 South Cass Avenue, Argonne, Illinois 60439-4833, USA.. Fcollart@anl.gov
SO BIOCHEMISTRY, (1999 Apr 13) 38 (15) 4691-700.
Journal code: A0G. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1ZFJ
EM 199907

L9 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
AN 1999322381 MEDLINE
DN 99322381
TI Differential signatures of bacterial and mammalian ***IMP*** ***dehydrogenase*** enzymes.
AU Zhang R; Evans G; Rotella F; Westbrook E; Huberman E; Joachimiak A; Collart F R

CS Biosciences Division, Argonne National Laboratory.
SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 537-43.
Journal code: C02. ISSN: 0929-8673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
EW 19991203

L9 ANSWER 3 OF 3 MEDLINE DUPLICATE 3
AN 1999322380 MEDLINE
DN 99322380
TI ***IMP*** ***dehydrogenase*** : structural aspects of inhibitor binding.
AU Goldstein B M; Colby T D
CS Department of Biochemistry and Biophysics, University of Rochester Medical Center, Rochester, NY, 14642, USA.. barry_goldstein@urmc.rochester.edu
SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 519-36. Ref: 118
Journal code: C02. ISSN: 0929-8673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199912
EW 19991203

=> d 1 14

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS
AN 1999:464100 CAPLUS
DN 131:83979
TI Method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** )
IN Collart, Frank R.; Huberman, Eliezer
PA The University of Chicago, USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9933996 | A1 | 19990708 | WO 1998-IB2109 | 19981223 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9915022 | A1 | 19990719 | AU 1999-15022 | 19981223 |
| PRAI | US 1997-997758 | | 19971224 | | |
| | WO 1998-IB2109 | | 19981223 | | |

RE.CNT 5
RE
(1) American Cyanamid Co; EP 0608722 A 1994
(2) Balzarini And De Clercq; BIOCHEMICAL JOURNAL 1992, V287, P785
(3) Carr; JOURNAL OF BIOLOGICAL CHEMISTRY 1993, V268(36), P27286 CAPLUS
(4) Pankiewicz; PHARMACOLOGY AND THERAPEUTICS 1997, V76(1-3), P89 CAPLUS
(5) Vertex Pharma; WO 9741211 A 1997

=> d kwic 1

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AB ***IMP*** ***dehydrogenase*** ( ***IMPDH*** ) is an essential enzyme that catalyzes the first step unique to GTP synthesis. To provide a basis for the evaluation of ***IMPDH*** inhibitors as antimicrobial agents, we have expressed and characterized ***IMPDH*** from the pathogenic bacterium ***Streptococcus*** ***pyogenes*** . Our results show that the biochemical and kinetic characteristics of S. ***pyogenes*** ***IMPDH*** are similar to other bacterial ***IMPDH*** enzymes. However, the lack of sensitivity to mycophenolic acid and the Km for NAD (1180 microM) exemplify some of the differences between the bacterial and mammalian ***IMPDH*** enzymes, making it an attractive target for antimicrobial agents. To evaluate the basis for these differences, we determined the ***crystal*** ***structure*** of the bacterial enzyme at 1.9 A with substrate bound in the catalytic site. The structure was determined using selenomethionine-substituted. . . obtained with synchrotron radiation from the undulator beamline (19ID) of the Structural Biology Center at Argonne's Advanced Photon Source. S. ***pyogenes*** ***IMPDH*** is a tetramer with its four subunits related by a crystallographic 4-fold axis. The protein is composed of two domains:. . . and a cystathione beta-synthase (CBS) dimer domain of so far unknown function. Using information provided by sequence alignments and the ***crystal*** ***structure*** , we prepared several site-specific mutants to examine the role of various active site regions in catalysis. These variants implicate the. . . flap as an essential catalytic element and indicate there are significant differences in the catalytic environment of bacterial and mammalian ***IMPDH*** enzymes. Comparison of the structure of bacterial ***IMPDH*** with the known partial structures from eukaryotic organisms will provide an explanation of their distinct properties and contribute to the design of specific bacterial ***IMPDH*** inhibitors.
CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
Catalytic Domain
Crystallography, X-Ray
Dimerization
Enzyme Inhibitors: PD, pharmacology
****IMP Dehydrogenase: CH, chemistry***
*** IMP Dehydrogenase: GE, genetics***
*** IMP Dehydrogenase: ME, metabolism***
Models, Molecular
Mutagenesis, Site-Directed
Protein Conformation
Recombinant Proteins: CH, chemistry
Recombinant Proteins: GE, genetics
Recombinant Proteins: ME, metabolism
****Streptococcus pyogenes: EN, enzymology***

CN EC 1.1.1.205 ( ***IMP*** ***Dehydrogenase*** ); 0 (Enzyme Inhibitors); 0 (Recombinant Proteins)

=> d kwic 1 14

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS
TI Method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** )
AB This invention relates to methods to identify specific inhibitors of the purine nucleotide synthesis enzyme, ***IMPDH*** . ***IMPDH*** is an essential enzyme found in all free-living organisms from humans to bacteria and is an important therapeutic target. The invention allows the identification of specific inhibitors of any ***IMPDH*** enzyme which can be expressed in a functional form in a recombinant host cell. To illustrate the utility of the invention, the coding sequence of human and ***Streptococcus*** , ***pyogenes*** ***IMPDH*** were cloned into the pJF118EH expression vector. A variety of eukaryotic or prokaryotic host systems commonly used for the expression. . . prodn. Utilization of exogenous guanosine as a control component of the methods allows for the identification of inhibitors specific for ***IMPDH*** rather than other causes of decreased cell proliferation.
ST inhibitor ***inosine*** ***monophosphate*** ***dehydrogenase*** human
IT Escherichia coli
(H712, expression host; method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT ***Streptococcus*** ***pyogenes***
(IMP-encoding gene from; method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT Bacillus subtilis
Bacteria (Eubacteria)
Eukaryote (Eukaryotae)
Insect (Insecta)
Neurospora
(expression host; method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT Drug screening
Molecular cloning
(method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT Drosophila
(serani; method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT 118-00-3, Guanosine, biological studies
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(as a control component; method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT 9028-93-7, ***Inosine*** ***monophosphate*** ***dehydrogenase***
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))
IT 367-93-1
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method to identify specific inhibitors of ***inosine*** ***monophosphate*** ***dehydrogenase*** ( ***IMPDH*** ))

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L8 18 S L1 AND L3 AND ((CRYSTAL OR X-RAY OR (X(W)RAY)) (3W) STRUCTU
L9 3 DUP REM L8 (15 DUPLICATES REMOVED)

=> s l4 and l17
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SEARCH ENDED BY USER

=> s l4 and l7

L10 0 L4 AND L7

=> s l4 and ((crystal or x-ray or (x(w)ray)) (3w) structur?)

3 FILES SEARCHED...
9 FILES SEARCHED...
L11 3 L4 AND ((CRYSTAL OR X-RAY OR (X(W) RAY)) (3W) STRUCTUR?)

=> dup rem l11

PROCESSING COMPLETED FOR L11
L12 3 DUP REM L11 (0 DUPLICATES REMOVED)

=> d 1-3

L12 ANSWER 1 OF 3 MEDLINE
AN 1999218077 MEDLINE
DN 99218077
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AU Zhang R; Evans G; Rotella F; Westbrook E; Huberman E; Joachimiak A; Collart F R
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SO CURRENT MEDICINAL CHEMISTRY, (1999 Jul) 6 (7) 537-43.
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L12 ANSWER 3 OF 3 MEDLINE
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TI ***IMP*** ***dehydrogenase*** : structural aspects of inhibitor binding.
AU Goldstein B M; Colby T D
CS Department of Biochemistry and Biophysics, University of Rochester Medical Center, Rochester, NY, 14642, USA.. barry_goldstein@urmc.rochester.edu
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Journal code: C02. ISSN: 0929-8673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
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EW 19991203

=> d ti au so abs 2-3

L12 ANSWER 2 OF 3 MEDLINE
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